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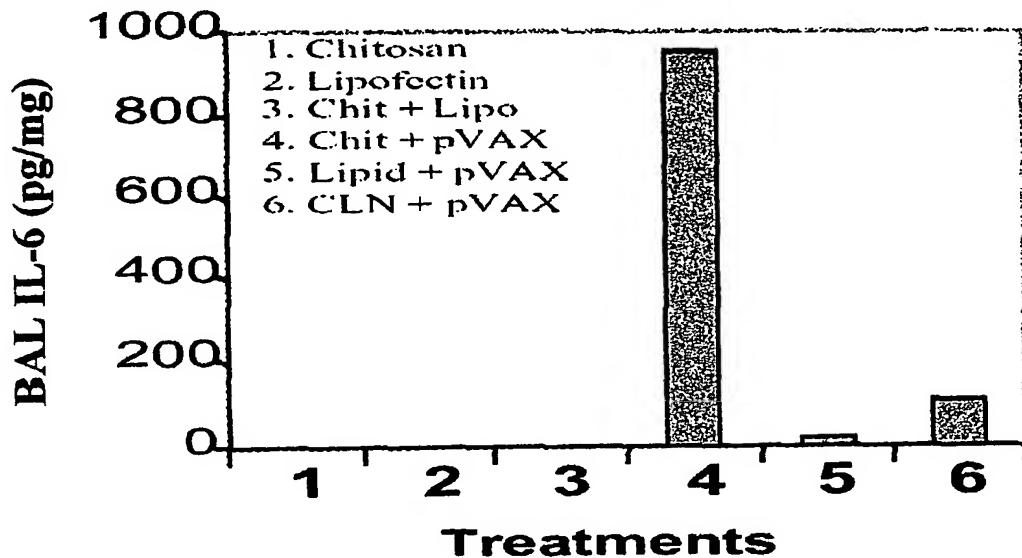
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[Continued on next page]

(54) Title: CHISTOSAN-MICROPARTICLES FOR IFN GENE DELIVERY



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(57) Abstract: The present invention provides particles comprising chitosan, or a derivative thereof, useful as delivery vehicles for polynucleotides encoding polypeptides, compositions comprising such particles and a pharmaceutically acceptable carrier, and methods for delivering polynucleotides using such particles. Optionally, the particles of the invention further comprise a lipid component. The present invention further provides a method for enhancing interferon-gamma expression to regulate the production of cytokines secreted by T-helper type 2 (Th2) cells within a subject by administering an effective amount of a particle of the subject invention to the subject, wherein the particle comprises a polynucleotide encoding interferon-gamma.



**Published:**

- *with international search report*
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# INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/US2004/004262

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 A61K47/36

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KUMAR M. ET AL: "Role of mucosal IFN-g gene transfer on allergic sensitization and RSV infection" J ALLERGY CLIN IMMUNOL, vol. 109, no. 1, 2002, page S4, XP008033852 abstract	1, 3-5, 7-10, 12-21
Y		1-23
X	HELLERLMAN G. ET AL: "Chitosan IFN-gamma gene nanosphere (CIN) therapy for allergic asthma: Modulation of specific T-cell and dendritic cell responses" J. ALLERGY CLIN IMMUNOL, vol. 111, no. 2, February 2003 (2003-02), page S265, XP008033841 abstract	1, 3-5, 7-10, 12-21
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the International filing date but later than the priority date claimed

\*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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\*&\* document member of the same patent family

Date of the actual completion of the international search

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31/08/2004

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## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/US2004/004262

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	KONG X. ET AL: "Chitosan IFN-gamma gene nanoparticle (CIN) therapy for allergic asthma in mice involves STAT4 signalling pathway" J ALLERGY CLIN IMMUNOL, vol. 111, no. 2, February 2003 (2003-02), page S354, XP008033853 abstract	1,3-5, 7-10, 12-21
X	WO 99/36089 A (LEONG KAM W ; TRUONG VU (US); AUGUST J THOMAS (US); UNIV JOHNS HOPKINS) 22 July 1999 (1999-07-22) claims 1,2,6; example 4	1,3-5,7, 8,10,12, 14-18,21
X	WO 97/20576 A (DANBIOSYST UK ; ILLUM LISBETH (GB)) 12 June 1997 (1997-06-12) claims 1,2,4	1,5,10, 15,16,21
X	WO 02/34287 A (PHARMEXA AS ; GAUTAM ANAND (DK); BEIER ANNE METTE (DK); MOURITSEN SOER) 2 May 2002 (2002-05-02) page 54, line 9 - page 57, line 15; claims 30,31,40	1,5,10, 15,21
X	HAMAJIMA K. ET AL: "Chitin micro-particles (CMP): a useful adjuvant for inducing viral specific immunity when delivered intranasally with an HIV-DNA vaccine" VIRAL IMMUNOLOGY, vol. 16, 2003, pages 541-547, XP008033839 see discussion abstract	1,5,10, 15,16,21
Y	DOW S W ET AL: "Systemic and local interferon gamma gene delivery to the lungs for treatment of allergen-induced airway hyperresponsiveness in mice" HUMAN GENE THERAPY, XX, XX, vol. 10, no. 12, 10 August 1999 (1999-08-10), pages 1905-1914, XP002241814 ISSN: 1043-0342 abstract page 1906, column 2, paragraphs 2,3; figures 2,5,6	1-23
		-/-

## INTERNATIONAL SEARCH REPORT

Int'l Application No  
PCT/US2004/004262

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>BEHERA A K ET AL: "Adenovirus-mediated interferon gamma gene therapy for allergic asthma: Involvement of interleukin 12 and STAT4 signaling"  <i>HUMAN GENE THERAPY</i>, XX, XX,      vol. 13, no. 14,      20 September 2002 (2002-09-20), pages      1697-1709, XP002241815      ISSN: 1043-0342      see discussion      abstract; figures 4,5</p>	1-23
X,P	<p>WO 03/028759 A (PEREZ DE LA CRUZ CH; CHEN LI-CHEN; HUANG SHAU-KU ; LEONG KAM W (US);      B) 10 April 2003 (2003-04-10)      page 15, lines 10-16      abstract; claims 18,19</p>	1,10,17, 21
T	<p>BIVAS-BENITA M ET AL: "Pulmonary delivery of chitosan-DNA nanoparticles enhances the immunogenicity of a DNA vaccine encoding HLA-A*0201-restricted T-cell epitopes of <i>Mycobacterium tuberculosis</i>"  <i>VACCINE</i>, BUTTERWORTH SCIENTIFIC.      GUILDFORD, GB,      vol. 22, no. 13-14,      16 April 2004 (2004-04-16), pages      1609-1615, XP004500413      ISSN: 0264-410X      abstract      see discussion      page 1613</p>	1,5,10, 15,17, 18,20,21

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2004/004262

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 1–23 partially because they relate to subject matter not required to be searched by this Authority, namely:  
**Although claims 11–20 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.**
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple Inventions in this International application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

**INTERNATIONAL SEARCH REPORT**

— information on patent family members —

Int'l Application No
PCT/US2004/004262

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